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*Original Research*

# CHA2DS2-VASc score is a predictor of angiographic high thrombus burden in patients with ST-Segment elevation myocardial infarction



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**Abstract**

Aim: High thrombus burden is an important indicator of complications that may occur in STEMI patients undergoing percutaneous coronary intervention. The CHA2DS2-VASc score is known as the score which is closely related to thrombosis. In this study, we aimed to investigate the association between CHA2DS2-VASc score and angiographic thrombus burden in patients with STEMI who underwent pPCI. Material and Method: A total of 570 consecutive STEMI patients who underwent pPCI were included in the study. The patients were divided into 2 groups: a high thrombus burden group and low thrombus burden group. The CHA2DS2-VASc scores were calculated for all patients. Results: The CHA2DS2-VASc scores were significantly higher in the high thrombus burden group, compared to the low thrombus burden group. Multivariate regression analysis showed that, prior MI history (odds ratio [OR] = 0.501, 95% confidence interval [CI]: 0.256-0.982, P =0.044), history of heart failure ( [OR] = 0.460, [CI]: 0.248-0.854, P = 0.014), CHA2DS2-VASc score ( [OR] = 1.812, [CI]: 1.369-2.400, P < 0.001) are predictors of high thrombus burden. Receiver–operating characteristics analysis revealed the cutoff value of CHA2DS2-VASc score ≥ 3 as a predictor of high thrombus burden with a sensitivity of 60.9% and a specificity of 75.0%. Discussion: In our study, we showed that CHA2DS2-VASc score is associated with high thrombus burden in STEMI patients who underwent primary PCI.

**Keywords**

CHA2DS2-VASc Score; STEMI; Primary PCI; TIMI Thrombus Grade

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## Introduction

Intracoronary thrombus plays an important role in the pathophysiology of ST-segment elevation myocardial infarction (STEMI) [1,2]. Despite the effectiveness of percutaneous coronary intervention (PCI), high thrombus burden is an important indicator of complications, that may occur in STEMI patients undergoing PCI [3]. Long-term adverse cardiovascular events of intracoronary thrombus burden remain a serious risk factor for stent thrombosis, distal embolization, and no-reflow [4-7]. Therefore, determination of the predictors of intracoronary thrombus may be helpful in the management of clinical and angiographic conditions.

CHA2DS2-VASc is a score known to be related with thromboembolism and is used in the estimation of the risk of development of thromboembolism in patients atrial fibrillation. The risk of thromboembolism increases with the CHA2DS2-VASc score [8]. However, previous studies have shown a association between CHA2DS2-VASc score, poor prognosis and acute coronary syndrome. CHA2DS2-VASc is associated with the incidence of stroke and thromboembolism, and this score is known to be closely correlated with thrombosis [9-11].

We aimed to investigate the association between CHA2DS2-VASc score and angiographic thrombus burden in patients with STEMI who underwent pPCI.

## Material and Method

A total of 570 consecutive STEMI patient who presented to our center and underwent pPCI between June 2015 and June 2016 were retrospectively examined. Patients with the presence of ST elevation of at least 1 mm (2 mm for V1-V3) in the two adjacent segments within the first 12 hours after the onset of symptoms or new onset of the left bundle branch block were included in the study. Patients with non-STEMI, unstable angina pectoris, those using oral anticoagulants, patients with hematological diseases, chronic inflammatory or autoimmune diseases were excluded from the study. The CHA2DS2-VASc score was calculated for each patient prior to PCI, and the relationship between the score and thrombus burden was investigated. The patients were divided into two groups according to thrombolysis in myocardial infarction (TIMI) grade: high thrombus burden (HTB) (TIMI 4 and 5) and low thrombus burden (LTB) (TIMI 0–3). All patients were given aspirin (300 mg) and clopidogrel (600 mg) as well as unfractionated heparin (70 IU / kg IV) at first medical contact. Glycoprotein IIb or IIIa inhibitor was applied in some patients according to the clinician's preference, but all patients received double antiplatelet therapy.

Age, sex, history of hypertension, history of diabetes mellitus, hyperlipidemia, smoking status, previous MI history, previous PCI or coronary artery bypass graft (CABG), history of heart failure, history of stroke and clinical risk factors were recorded for all included patients. Additionally, blood pressure, heart rate, Killip class, previous medications, the presence of preinfarction angina, pain to balloon time were recorded for all patients during hospital admission.

### *Definition*

Diagnosis of diabetes was established in the case of antidiabetic drug use, or when postprandial blood glucose was higher than 200 mg / dL or fasting plasma glucose was at least 126 mg/dL at any time [12]. Patients using antihypertensive drugs or having a systolic tension of 140 mmHg or a diastolic tension of 90 mmHg or higher measured during resting at different periods of time were defined as hypertensive [13]. Hyperlipidemia was defined as a total cholesterol level over 200 mg/dL, triglycerides level over 160 mg/dL, or low density lipoprotein level over 130 mg/dL [14]. Ejection fraction was calculated using the modified Simpson's method. Stenosis of ≥ 50% in noncoronary arteries was defined as peripheral arterial disease.

Based on the CHA2DS2-VASc score, patients were given 1 point for congestive heart failure, hypertension, being aged between 65 to 74 years, diabetes mellitus, vascular disease (prior MI, peripheral artery disease, aortic plaque) and female gender; and 2 points for being aged 75 years and over, and previous cerebrovascular events (Transient Ischemic Attack (TIA)/stroke) [8]. One point was added to the score in all patients considering that they were admitted with STEMI [15].

### *Angiography:*

Angiographic thrombus burden was scored as five grades as previously described by Gibson et al [16]. Grade 0: No angiographic evidence of thrombus; Grade 1: possible thrombus (reduced contrast density, haziness of contrast, irregular lesion contour, suggestive, but not firmly diagnostic of thrombus); Grade 2: firmly thrombus with severe filling defect and marked irregular lesion contour on more than one angiographic imagings (greatest dimension of thrombus < 1/2 vessel diameter); Grade 3: firmly presence of thrombus on all angiographic images (greatest dimension from > 1/2 to < 2 vessel diameters); Grade 4: firmly presence of great thrombus (greatest dimension > 2 vessel diameters) ; Grade 5: total occlusion of a vessel. The content of the occlusive thrombus need to be further investigated in order to detect Grade 5 TIMI thrombosis. A guide wire or a small balloon are advanced along the thrombotic total occlusion to provide restoration of the antegrade flow in the vessel. This enables restrafication of the underlying residual thrombosis during coronary angiography (final TIMI thrombograde) [17]. In our study, first TIMI thrombus grade was calculated based on the first imaging. In patients who had a grade 5 TIMI thrombus, underlying residual thrombus was restrained as a result of the restoration of antegrade flow through a guidewire or a small balloon (final TIMI thrombus-grade) [5,18]. Then the final TIMI grades were divided into two groups as LTB (0 to 3) and HTB (4 to 5). All TIMI thrombus scores were then evaluated by two experienced cardiologists, and the decision was made by consensus.

Written or verbal informed consent was received from all patients, and the study protocol was approved by the hospital's local ethics committee in accordance with the Helsinki Declaration and Good Clinical Practice Guidelines.

### *Statistical analysis:*

The data analysis was conducted using SPSS (version 20.0, SPSS Inc., Chicago, IL, USA) and MedCalc statistical software (trial version 12.7.8, Mariakerke, Belgium). Continuous variables data are expressed as the mean ± standard deviation. Categorical variables were compared using Chi-square or Fisher's

exact tests and summarised as percentages. The Kolmogorov–Smirnov test was used to evaluate the distribution of the continuous variables. In order to predict a high TIMI thrombus grade, age, gender, diabetes mellitus (DM), hypertension (HT), hyperlipidaemia (HL), smoking, preinfarct angina, time interval from pain to PCI, systolic and diastolic blood pressure, history of stroke, history of heart failure, history of prior MI, and Killip ≥ 3, stent length, stent diameter , pre-MI medication and CHA2DS2-VASc score were included in the univariate analysis. The parameters with p < 0.05 were included in the multiple logistic analysis.

Receiver operating characteristic (ROC) curves were used to predict the future incidence of high TIMI thrombus grade.

## Results

A total of 570 STEMI patients were included in the study (mean age 62.3 + 12.4 and 71.6% male). The calculated thrombus grades based on the first angiographic imaging, and the final TIMI thrombus grades obtained by restratification of the underlying residual thrombus in patients with TIMI thrombus grade 5 are given in Table 1. In conclusion, the final TIMI thrombus grades of the study population were low thrombus burden in 296 (51.9%), and high thrombus burden in 274 (48.1%) patients. Age, gender, hypertension, history of stroke or TIA, history of heart failure, pre-infarction angina pain-balloon time, EF, stent diameter, history of prior MI , CHA2DS2-VASc score and no-reflow, were statistically different in the group of a high-thrombus burden compared to the low-thrombus burden group. The clinical characteristics as well as the angiographic and PCI features of the findings are listed in Table 2.

Among the significant parameters in the univariate analysis (age, gender, history of prior MI, hypertension, history of stroke/TIA, history of heart failure, pain to –PCI time, Killip class ≥ 3, setent diameter, CHA2DS2-VASc score), those which were also found to be significant in the multiple regression analysis included prior MI history (odds ratio [OR] = 0.501, 95% confidence interval [CI]: 0.256 - 0.982, *P* = 0.044), History of Heart Failure ( [OR] = 0.460, [CI]: 0.248-0.854, *P* = 0.014), CHA2DS2-VASc score ( [OR] = 1.812, [CI]: 1.369-2.400, *P* < 0.001) (Table 3).

The optimal threshold CHA2DS2-VASc score for predicting high- thrombus bureden was ≥ 3, with a 60.9% sensitivity and 75.0% specificity (area under the curve [AUC]: 0.725, 95% CI: 0.683 – 0.767, *P* < 0.001) (Figure 1).

## Discussion

In our study, history of heart failure, history of prior MI and CHA2DS2-VASc score was found to predict the development of high- thrombus burden in STEMI patients who underwent to PCI. In addition, the CHA2DS2-VASc score has been shown sensitive to the prediction of the development of high thrombotic burden. (AUC: 0.725).

Coronary artery thrombus is the main pathophysiological event of acute myocardial infarction, which develops after a plaque rupture, causing partial or complete occlusion of the coronary artery [19]. The amount of intracoronary thrombus burden is among the determinants of prognosis in STEMI [4,5]. Intracoronary thrombus decreases coronary blood flow depending on partial or complete occlusion. Accordingly, distal embolizations developing due to the pieces which are broken spontaneously or during PCI lead to myocardial damage [19]. Supporting this, Tandoğa et al. showed lower TIMI flow and less myocardial blush due to distal embolization following PCI in patients with a high thrombus burden [17].

The CHA2DS2-VASc score includes risk factors with proven sensitivity in the prediction of the risk for thromboembolism and stroke in patients with atrial fibrillation [8,20]. Stroke and transient ischemic attack may occur due to nonatherosclerotic vascular pathologies as well as thromboembolism and atherosclerosis [21]. In addition to its use in atrial fibrillation, the CHA2DS2-VASc score has been defined as an appropriate and helpful predictor of the vascular events such as coronary stenosis followed by MI, stroke, and death before coronary angiography in patients with acute coronary syndrome [22,23]. Again, the CHA2DS2-VASc score has been shown to be associated with atrial and ventricular arrhythmias, newly developed heart failure, and sudden cardiac death after STEMI [24]. Ipek et al. showed an association between CHA2DS2-VASc score and no-reflow [25]. However, in that study thrombus burden which is known to play an important role in the development of noreflow was not mentioned. In our study, we found an association between CHA2DS2-VASc score and high thrombus burden and in patients with higher thrombus burden developed higher noreflow. Supporting the previous studies, this result suggests that CHADS2 VASc score may be indirectly associated with the

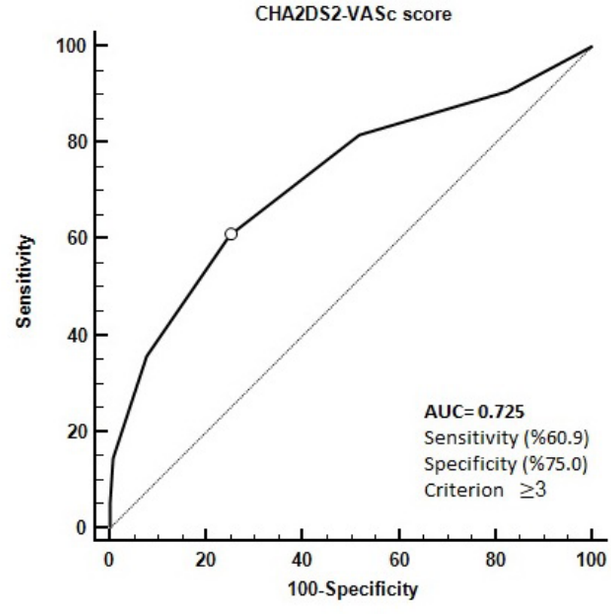


Figure 1. ROC curve graphics to detect the best cut-off value for the CHA2DS-2VASc score in predicting the high thrombus burden in STEMI patients.

Table 1. Initial TIMI Thrombus Burden Classification and Final TIMI Thrombus Burden Reclassification.

| | Initial TIMI Thrombus Burden Classification | Final TIMI Thrombus Burden Reclassification |
|---|---|---|
| Grade 0, n and % | 6 (1.1) | 9 (1.6) |
| Grade 1, n and % | 15 (2.6) | 29 (5.1) |
| Grade 2, n and % | 17 (3.0) | 83 (14.6) |
| Grade 3, n and % | 113 (19.8) | 175 (30.7) |
| Grade 4, n and % | 45 (7.9) | 252 (44.2) |
| Grade 5, n and % | 374 (65.6) | 22 (3.9) |

Table 2. Clinical Characteristics and Angiographic and PCI Features of the Findings in Two Groups

| | | Low Thrombus Burden (n=296) | High Thrombus Burden (n=274) | p |
|---|---|---|---|---|
| Age (years) | | 59.7±11.1 | 65.2±13.1 | <0.001 |
| Sex (% female) | | 65(22) | 97(35.4) | <0.001 |
| Diabetes Mellitus n (%) | | 92(31.1) | 95(34.7) | 0.373 |
| Hypertension n (%) | | 147(49.7) | 176(64.2) | <0.001 |
| Smoking n (%) | | 129(43.6) | 113(41.2) | 0.572 |
| History of stroke/TIA, n (%) | | 5(1.7) | 18(6.6) | 0.003 |
| History of heart failure n (%) | | 23(7.8) | 65(23.7) | <0.001 |
| Pre-infarction angina | | 65(22.0) | 69(25.2) | 0.365 |
| SBP (mmHg) | | 135±30 | 134±36 | 0.884 |
| DBP (mmHg) | | 80±18 | 79±21 | 0.656 |
| Heart Rate (p/min) | | 76±15 | 75±16 | 0.993 |
| Pain to- PCI time | | 195±111 | 218±115 | 0.016 |
| Kilip ≥ 3 n (%) | | 16(5.4) | 28(10.2) | 0.031 |
| Stent leght (mm) | | 21.0±8.5 | 22.4±10.0 | 0.069 |
| Stent Diameter (mm) | | 3.1±0.3 | 3.0±0.3 | 0.038 |
| Ejection Fraction % | | 48.7±7.6 | 46.2±8.1 | <0.001 |
| B-blocker n (%) | | 49(16.6) | 40(14.6) | 0.520 |
| CCB n (%) | | 16(5.4) | 23(8.4) | 0.158 |
| Statin n (%) | | 68(23) | 64(23.4) | 0.913 |
| Aspirin n (%) | | 47(17.2) | 45(15.2) | 0.527 |
| PAD n (%) | | 15(5.1) | 23(8.4) | 0.198 |
| History of Prior MI n (%) | | 27(9.1) | 63(23) | <0.001 |
| History of Prior PCI n (%) | | 36(12.2) | 38(13.9) | 0.545 |
| CABG n (%) | | 8(2.7) | 15(5.5) | 0.093 |
| Noreflow n (%) | | 15(5.1) | 28(10.2) | 0.020 |
| CHA2DS2VASc score | | 2.38±1.25 | 3.22±1.68 | <0.001 |
| IRA | LMCA | 1 | - | - |
| | LAD n (%) | 143(50.4) | 141(51.5) | |
| | CX n (%) | 38(12.8) | 31(11.3) | |
| | RCA n (%) | 110(37.2) | 94(34.3) | |
| | Other n (%) | 5(1.7) | 5(1.8) | |

CABG: Coronary Artery Bypass Greft, CCB: Calcium Channel Blocker, CX: Circumflex Artery, DBP: Diastolic Blood Pressure, IRA: Infarct Related Artery, LM: Left Main, LAD: Left Ascending Artery, MI: Myocardial Infarction, PAD: Peripheral Artery Disease, PCI: Percutaneous Coronary Intervention, RVA: Right Coronary Artery, SBP: Systolic Blood Pressure. TIA: Transient Ischemic Attack ,

Table 3. Univariate and Multivariate Logistic Regression Analysis to Detect the Independent Predictors of High TIMI Thrombus Burden

| | Univariate analysis | | Multivariate analysis | | |
|---|---|---|---|---|---|
| | OR (95%CI) | P value | OR | 95% CI | P value |
| Age | 1.038 (1.024-1.053) | <0.001 | | | |
| Sex | 1.948 (1.345-2.820) | <0.001 | | | |
| History of Prior MI | 2.975 (1.831-4.834) | <0.001 | 0.501 | 0.256-0.982 | 0.044 |
| Hypertension | 1.820 (1.301-2.547) | <0.001 | | | |
| History of Stroke | 2.023 (1.224-3.343) | <0.001 | | | |
| History of Heart Failure | 3.691 (2.220-6.138) | <0.001 | 0.460 | 0.248-0.854 | 0.014 |
| Pain to –pcı time | 1.002 (1.000-1.003) | 0.016 | | | |
| Kilip Class ≥3 | 0.502 (0.265-0.950) | 0.031 | | | |
| Stent Diameter | 0.615 (0.387-0.978) | 0.040 | | | |
| CHA2DS2VASc score | 1.851(1.617-2.119) | <0.001 | 1.812 | 1.369-2.400 | <0.001 |

development of noreflow [25]. Ünal et al. demonstrated a relationship between acute stent thrombosis and CHA2DS2-VASc score in patients without atrial fibrillation [15]. In our study, CHA2DS2-VASc score was demonstrated to be an independent predictor of high thrombus burden. CHA2DS2 -VASc score may lead to poor results such as high thrombus burden because it involves such factors as including DM, HT, advanced age, and heart failure. F. Scudiero et al demostrated a relationship between CHA2DS2-VASc score and high platelet reactivity [26]. In addition, the association between CHA2DS2-VASc score and acute stent thrombosis, noreflow, and thromboembolism and thrombosis in atrial fibrillation, which has been demonstrated in the previous studies may be helpful to explain the reason of its association with high thrombus burden in STEMI patients [8,15,25]. Again for the same reasons, we think it is not surprising to observe that CHADS VASc is a predictor of the development of high thrombus burden.

*Study Limitation*

Our study was designed as a single center and retrospective study. Again, stratification of thrombus burden based on visual assessment may have some limitations. Intravascular ultrasonography (IVUS) and Optik Koherans Tomografi (OCT) confirm thrombus in relation with (ruptured) atherosclerotic plaque in a large proportion of STEMI. In our study OCT and IVUS is not used. MI and PAD were included in the definition of vascular disease during the study. Patients with complicated aortic plaque could not be evaluated. Therefore, calculation of CHADS2-VASc score in STEMI patients may be considered as a limited situation.

*Conclusion:*

In our study, we demonstrated that CHADSVASc, which can be easily calculated in STEMI patients predicts high thrombus burden before the procedure. We believe that CHA2DS2-VASc score may be helpful for clinicians in practice in order to estimate high thrombus burden pre-procedure and take the necessary measures. However, it would be appropriate to test the CHA2DS2-VASc score in a wider range and prospective studies with different populations.

*Scientific Responsibility Statement*

*The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.*

*Animal and human rights statement*

*All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. No animal or human studies were carried out by the authors for this article.*

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*Conflict of interest*

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